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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/808,124	POTTER ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2004 and 03 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *91-101,103,107 and 110-120* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *91-101,103,107 and 110-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/10/03, 5/3/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 20, 2004 has been entered.

2. Claims 11-22 and 63-120 were previously pending. In an amendment filed January 20, 2004 Applicants cancelled claims 11-22, 63-90, 102, 104-106, 108 and 109 and amended claims 91, 103, 107, 110, 111, 116 and 117. Claims 91-101, 103, 107 and 110-120 are pending and will be examined.

3. As indicated in the Advisory Action mailed February 5, 2004, Applicants' claim cancellations, amendments and arguments overcame the following rejections: rejection under 35 U.S.C. 112, first paragraph, written description, for claims 11-22, 63-90, 102, 104-106, 108, 109 (claims cancelled); rejection under 35 U.S.C. 112, first paragraph, enablement, for claims 11-22 and 63-120 (claims 11-22, 63-90, 102, 104-106, 108 and 109 were cancelled); rejection under 35 U.S.C. 102(a) for claims 71, 82, 91 and 102 (claims 71, 82 and 102 cancelled, claim 91 amended).

4. Applicants' arguments filed January 20, 2004 were addressed in the Advisory Action mailed February 5, 2004. The arguments presented in the Reply filed May 3, 2004 are addressed in the "Response to Arguments" section below.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on May 3, 2004 was filed after the mailing date of the Advisory Action on February 5, 2004. The submission is in compliance with the

provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

6. Regarding the IDS filed on April 10, 2003, Applicants arguments regarding the reference of English translation of the Japanese patent were considered persuasive. The reference has been considered and a copy of the page will be mailed to Applicants with this office action.

Priority

7. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 91, 107, 110, 112, 113, 117 and 118 of this application.

Claims 91 and 107 are drawn to an MMLV reverse transcriptase comprising a mutation in Phe309, claim 110 is drawn to the mutation where Phe309 is replaced with asparagine. Claims 112, 113, 117 and 118 are drawn to a reverse transcriptase comprising a mutation at Asp544. The provisional application No. 60/189,454, filed March 15, 2000, provides no support for these limitations, therefore the priority date for these claims is the filing date of the instant application, March 15, 2001.

Response to Arguments

8. Applicant's arguments filed May 3, 2004 have been fully considered but they are not persuasive. Regarding the rejection of claims 91-101, 103, 107 and 110-120 under 35 U.S.C. 112, first paragraph, written description, Applicants argue that:

A) the *Eli Lilly* decision was overturned in the *Amgen* case (response, page 3, last two paragraphs, page 4, page 5, first paragraph),

B) the specification describes a broad genus of enzymes that could serve as backbone for making the claimed amino acid substitutions and these backbone sequences do not need to be provided in the specification because they were known.

Regarding A), when Applicant cites *Amgen*, Applicant is twisting this decision away from the central decisive point in the case. The Federal Circuit in Amgen stated "Thus, the undisclosed element TKT urges invalidates Amgen's product claims is a different method (endogenous activation) of making the claimed compositions. But, as the district court noted, under our precedent the patentee need only describe the invention as claimed, and need not describe an unclaimed method of making the claimed product." So in Amgen, the written description rejection was found not to apply because there were other methods of making the product, but the product itself was fully described. Here, the situation is entirely different. The product is not described. There are literally no structural requirements imposed by the claims whatsoever.

Applicants rely upon the conservation among retroviral reverse transcriptases. However the claim permits ANY SEQUENCE that has reverse transcriptase activity. Since any series of mutations is permitted by this claim, one can change any "retroviral" reverse transcriptases into any other reverse transcriptases with sufficient modifications or mutations. In fact, any protein can be changed into any other protein by the appropriate selection of mutations or modifications. Finally, as noted in the rejection, claim 91 defines the reverse transcriptase solely by function. This is expressly found inadequate in *Lilly* to define the genus and provide possession. The current case demonstrates an instance, as in *Lilly*, where the absence of a precise definition of the genus, here reverse transcriptases which are modified to have certain functions, is insufficient to comply with the requirement for written description. See Id. at 1569, 43 U.S.P.Q.2d at 1405. The patentee's claims in *Lilly* were drawn to a large genus of all vertebrate or all mammalian insulin cDNA, while

the specification of the patents only provided the cDNA sequences for the rat or human insulin proteins. See Id. at 1563, 43 U.S.P.Q.2d at 1401. *Lilly* held that a generic claim limitation which involved chemical formula were usually properly described. However, in the case of materials identified solely by function with chemical structure, the Federal Circuit stated that "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is." Id. at 1568, 43 U.S.P.Q.2d at 1406. Here, the definition of the reverse transcriptases operates solely on the basis of what the enzymes do, rather than what they are.

Regarding B), when Applicant argues that other enzymes could serve as the backbone for the claimed reverse transcriptases, Applicant is arguing a limitation that is not in the claims. There is no limitation in the claims which requires any particular reverse transcriptase to serve as the backbone of the claimed enzyme. So there is no structural element imposed by the "backbone" because no "backbone" is required. None of the language in the claim provides any description of anything specific whatsoever. The claim is to an undefined genus to which an infringer not only will be uncertain if they are infringing, but more importantly, uncertain what are the bounds of the material claimed. The central aspect of patent examination is to set out clear boundaries for the public, for potential infringers and for the reviewing bodies. In this case, these claims fail to set out any bounds at all. Without any structural limitations whatsoever, the claims are not described in a manner which complies with 35 U.S.C. 112, first paragraph.

There are few clearer situations of the problem recognized in *Lilly*, "Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." The material claimed by Applicant may be capable of synthesis. However, when there are literally no structural constraints on the material so

that the ordinary practitioner not only does not know, but cannot know, what reverse transcriptases properly fall within the scope of the claims, the claims fail to meet the written description requirement.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 91-101, 103, 107 and 110-120 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of proteins which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. As discussed above, the claims essentially read on any reverse transcriptases whatsoever. There is no description in the specification of any MMLV reverse

transcriptases which differ in sequence from the known prior art sequence. The claims are drawn to particular positions mutated in the claimed reverse transcriptases (e.g., Tyr 64, Arg 116, Lys 152, Gln 190, Thr 197 and Phe 309) and clearly read on any reverse transcriptase from any organism without the sequences of those enzymes being taught or suggested in the specification. The broadest claim is drawn to any reverse transcriptase from any species with any sequence and any mutation. Thus the claims encompass a genus which comprises hundreds of millions of different possibilities since in a protein of about 684 amino acids there are more than 684^{19} possible single amino acid changes. The number of possible changes becomes even more astronomical if multiple amino acid changes are permitted. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains are required. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, proteins which have a removable amino terminal end.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the MMLV reverse transcriptases lack any specific structure, which is precisely the situation of naming a type of material which is generally known to

be likely exist, but, except for the wild type protein with the exemplified mutations, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to any reverse transcriptase which is modified for enhanced fidelity. In particular, while the claims define particular amino acids, such as the Y64W change (claim 93), the entire surrounding sequence of 683 amino acids is not defined in these claims, leaving only the particular change as a fixed point in what can be a protein of any sequence.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a reverse transcriptase with enhanced fidelity, without sufficient structure to meet this functional limitation.

In the instant application, certain specific reverse transcriptases are described implicitly, though not explicit teaching of the complete sequence of a particular MMLV reverse transcriptase is found in the specification. Applicants describe mutational studies of Superscript II, a mutant of the Moloney Murine Leukemia Virus reverse transcriptase (M-MLV RT), which had the following mutations in the RNAse H domain: Asp524->Gly, Asp583->Asn, Glu562->Gln (page 50, [0136], page 52, [0139]). Applicants provided information that the RNAse H domain mutations were introduced into a clone pRT601, which was described in the following patents: 5,244,797; 5,405,776; 5,668,005 and 6,063,608. As described in the '797 patent, column 12, lines 53-64, the pRT601 clone contained an RT gene in which the amino-terminal part was from an M-MLV RT, and the carboxy terminus was "similar to the viral enzyme". Therefore, the starting material for the

mutational analysis of the M-MLV RT wasn't even an M-MLV RT enzyme, but a synthetic construct. In addition, Applicants did not provide any evidence that the point mutations introduced into the pRT601 vector did indeed reduce the RNAse H activity of the reverse transcriptase. Furthermore, it is unclear whether the Superscript II enzyme had all three of the point mutations, or whether there were different versions of the Superscript II with one point mutation in each of them or with pairwise combinations of such mutations.

To summarize this part, Applicants were not is possession of an M-MLV RT enzyme as a starting material for further mutational studies, and point mutations introduced into the RNAse H domain of a 684 amino acid reverse transcriptase encoded by the pRT601 vector (further referred to as pRT601 RT) were not proven to possess reduced RNAse H activity. It is also not clear what was the starting material for further mutational analysis.

Applicants then proceeded to introduce mutations into the Superscript II enzyme. The following facts are presented in the specification: 1) mutations Y64W, R116M, K152R, Q190F, T197A and V223H resulted in RTs with increased fidelity and lower degree of nucleotide misincorporation (Table 2, [0140], [0141]); 2) mutations F309N, T197E and Y133A resulted in RTs with decreased TdT activity ([0142], [0149]), 3) mutant RTs with H204R+Y306K, H204R+Y306K +F309N mutations had increased fidelity ([0142]), and 4) mutations F309N and F309N/V223H had increased fidelity as well. The specification does not provide reasoning why these residues were chosen for making changes and how the choice of replacement amino acid was decided. The Applicants have not described any other mutations of Y64, R116, K152, Q190, T197 and V223 that result in increased fidelity. In terms of H204R, Y306K, and F309N mutations, only two of their possible combinations, H204R+Y306K, H204R+Y306K +F309N, were shown to impart increased

fidelity on the enzyme, but no evidence was provided that any of those mutations alone or in any other combination resulted in increased fidelity.

Therefore, claims 91-101, 103, 107 and 110-120 encompass a genus of all possible reverse transcriptases, including allelic variants such as insertions, deletions and mutations, and no specific amino acid sequences of any such protein or nucleic acids encoding them, including the starting material, has been presented in the specification. Thus, the definition of an M-MLV reverse transcriptase lacks any specific structure, with the protein defined solely by its function. While some mutations are defined, such as the ones cited above, the rest of the surrounding sequence of 683 amino acids is not defined. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any proteins other than those expressly disclosed which comprise the MMLV reverse transcriptase encoded by the pRT601 vector and modified at the selected positions as having enhanced fidelity. Therefore, the claims fail to meet the written description requirement by encompassing proteins which are not described in the specification.

Claim Rejections - 35 USC § 112, first paragraph, new matter

11. Claims 112, 113, 117 and 118 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

Claims 112, 113, 117 and 118 contain a limitation of a mutation in Asp 544. There is no support in the specification for this limitation. In Example 1 on page 52, Applicants list mutations which were made in M-MLV RT gene to remove RNAse H activity, and these were D524G, D583N and E562Q. No Asp544 is mentioned.

Therefore, this limitation represents new matter.

Claim Interpretation

12. As a preliminary matter, the following is how the claims are interpreted for purposes of the 35 U.S.C 112, second paragraph, and prior art rejections. Claim 91 requires MMLV reverse transcriptases comprising, for example, a modification at the position corresponding to Tyr 64 of the MMLV reverse transcriptase. That is, the protein must have reverse transcriptases activity, and narrowly interpreted, the protein cannot have, for example, a tyrosine at position 64. However, the claim is not limited to requiring a tyrosine at position 64, for example, since in some reverse transcriptases, the natural sequence is an amino acid other than tyrosine at position 64. In those reverse transcriptases, the mutation language requires a different amino acid than wild type. So these claims actually read on any active reverse transciptase enzyme whatsoever, since the amino acids surrounding the particular residues are not restricted to belong to any particular sequence, and, therefore, they do not possess any other structural constraints.

Claim Rejections - 35 USC § 112, second paragraph

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 111-115 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 111-115 are indefinite in claim 111. Claim 111 is indefinite over the recitation of "said reverse transcriptase has substantially reduced RNAse H activity". It is not clear how this activity is determined, i.e. with respect to what standard. Applicants provide the following description on page 24, [0070]:

"Preferred enzymes for use in the invention include those that are reduced or substantially reduced in RNase H activity. Such enzymes that are reduced or substantially reduced in RNase H activity may be obtained by mutating the RNase H domain within the reverse transcriptase of interest, preferably by one or more point mutations, one or more deletion mutations, and/or one or more insertion mutations as described above. By an enzyme "substantially reduced in RNase H activity" is meant that the enzyme has less than about 30%, less than about 25%, 20%, more preferably less than about 15%, less than about 10%, less than about 7.5%, or less than about 5%, and most preferably less than about 5% or less than about 2%, or which lacks the RNase H activity of the corresponding wildtype or RNase H enzyme such as wildtype Moloney Murine Leukemia Virus (M-MLV), Avian Myeloblastosis Virus (AMV) or Rous Sarcoma Virus (RSV) reverse transcriptases."

However, claim 91 encompasses reverse transcriptases for which there is no fixed structure, i.e., amino acid sequences, therefore it is indefinite what structure should be compared to the

claimed reverse transcriptases for purposes of being "wild type". For example, claim 91 encompasses a class of reverse transcriptases which may be constructed by putting together domains from two or more different reverse transcriptases or any other proteins, for example, HIV-1 RT and AMV RT, and then mutating some of the residues in both parts. For the purpose of determining RNAse H activity, what is the "wild type" enzyme: HIV-1 RT, AMV RT or the fusion protein?

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. The rejections presented below are based on different interpretations of the term "MMLV reverse transcriptase" in claim 91. Rejection over Kotewicz et al. is based on a literal interpretation of this term. The rejection over Hizi et al. is based on the interpretation of the MMLV reverse transcriptase as a reverse transcriptase which contains some amino acids from MMLV sequence, and rejection over Georgiadis et al. is based on the broadest interpretation of claim 91, namely, requiring that residues 64, 116, 152, 190, 197 and 309 be different from tyrosine, arginine, lysine, glutamine, threonine or phenylalanine, respectively, but the rest of the protein does not have to be derived in any way from MMLV.

17. Claims 91, 92, 94, 96, 98, 100, 107, 111 and 116 are rejected under 35 U.S.C. 102(b) as being anticipated by Kotewicz et al. (U.S. Patent No. 5,244,797; cited in the IDS).

Regarding claims 91 and 92, Kotewicz et al. teach an MMLV reverse transcriptase with a glutamine at position 64 (Fig. 6a).

Regarding claims 91 and 94, Kotewicz et al. teach an MMLV reverse transcriptase with a leucine at position 116 (Fig. 6a).

Regarding claims 91 and 96, Kotewicz et al. teach an MMLV reverse transcriptase with an asparagine at position 152 (Fig. 6a).

Regarding claims 91 and 98, Kotewicz et al. teach an MMLV reverse transcriptase with an alanine at position 190 (Fig. 6a).

Regarding claims 91 and 100, Kotewicz et al. teach an MMLV reverse transcriptase with a glutamate at position 197 (Fig. 6a).

Regarding claims 91 and 107, Kotewicz et al. teach an MMLV reverse transcriptase with a valine at position 309 (Fig. 6a).

Regarding claims 111 and 116, Kotewicz et al. teach an MMLV reverse transcriptase with substantially no RNAse H activity (col. 8, lines 63-67). The mutations causing decrease in RNAse H activity were deletions in the C-terminus of the protein, therefore, they would change the amino acids 544, 562 and 583 by deleting them (col. 15, lines 1-34).

18. Claims 91, 92, 94, 96, 98, 100, 107, 111, 112, 116 and 117 are rejected under 35 U.S.C. 102(b) as being anticipated by Hizi et al. (Virology, vol. 175, pp. 575-580, 1990), as evidenced by Schatz et al. (FEBS Letters, vol. 257, pp. 311-314, 1989).

Hizi et al. teach fusion proteins between the MMLV reverse transcriptase (RT) and HIV-1 RT (Table 1, Fig. 2).

Regarding claims 91, 92, 94, 96, 98, 100, Hizi et al. teach a mutant HM-2 with 317 N-terminal amino acids of HIV-1 RT and 302 C-terminal amino acids of MMLV RT. Therefore, as

evidenced by Fig. 1 of Schatz et al., position 64 of the fusion reverse transcriptase is now a lysine, position 116 a phenylalanine, position 152 a glycine, position 190 a glycine and position 197 a glutamine.

Regarding claims 91, 107, 111, 112, 116 and 117, Hizi et al. teach a mutant MH-3 with 212 N-terminal amino acids of MMLV RT and 441 C-terminal amino acids of HIV-1 RT. Therefore, residue 309 in this protein is no longer a phenylalanine. Further, residues 544, 583 and 562 are the residues of HIV-1 RT, not MMLV RT. Again, from Fig. 1 of Schatz et al., residue 120 of the HIV-RT will become residue 213 of the fusion transcriptase, and residue 544 in the fusion transcriptase is now a lysine, residue 562 a leucine and residue 583 a glycine, therefore, they are not Asp, Glu or Asp, respectively. This mutant has no RNAse H activity.

19. Claims 91, 92, 94, 96, 98 and 100 are rejected under 35 U.S.C. 102(b) as being anticipated by Goergiadis et al. (Structure, vol. 3, pp. 879-892, 1995; cited in the IDS).

Georgiadis et al. teach an HIV-1 reverse transcriptase, which has a lysine at position 64, phenylalanine at position 116, glycine at position 152, glycine at position 190 and glutamine at position 197 (Fig. 3).

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 91, 92, 96 and 107are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 3, 5 and 6 of copending Application No. 10/661,819. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 2, 3, 5 and 6 are species of claims 91, 92, 96 and 107.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Specifically, claim 91 of the current application is drawn to an MMLV reverse transcriptase comprising at least one mutation at an amino acid position selected from the group consisting of Tyr64, Arg116, Lys152, Gln190, Thr197 and Phe 309, whereas claim 2 of the 10/661,819 application is drawn to an MMLV reverse transcriptase which has been modified or mutated to increase or enhance thermostability, and which has one or more modifications at positions corresponding to Leu52, Tyr 64, Lys152, His204, Met289, Thr306 and Phe309. Therefore, claim 2 of the 10/661,819 is a species of claim 91 in that it contains an added limitation of increased or enhanced thermostability.

Further, claim 5 of the 10/661,819 application is a species of claim 92, since it is drawn to a tyrosine 64 being replaced with arginine and claim 6 of the 10/661,819 application is a species of claim 96, since it is drawn to a lysine 152 being replaced with methionine.

Therefore, claims 91, 92, 96 and 107 of the instant application are generic to claims 2, 3, 5 and 6 of the 10/661,819 application, or, in other words, claims 91, 92, 96 and 107 of the instant application are anticipated by claims 2, 3, 5 and 6 of the 10/661,819 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

3. Claims 91, 100, 107, 110, 111, 112, 114, 115, 117, 119 and 120 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19, 20, 22, 23, 25, 26, 28 and 29 of copending Application No. 09/845,157. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 19, 20, 22, 23, 25, 26, 28 and 29 of copending Application No. 09/845,157 are species of claims 91, 100, 107, 110, 111, 112, 114 115, 117, 119 and 120 of the instant application.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Specifically, claim 91 of the current application is drawn to an MMLV reverse transcriptase comprising at least one mutation at an amino acid position selected from the group consisting of Tyr64, Arg116, Lys152, Gln190, Thr197 and Phe 309, whereas claim 19 of the 09/845,157 application is drawn to an MMLV reverse transcriptase with amino acid substitutions at positions Leu52, His204, Met289, Thr306, Tyr133, Thr197 or Phe309 and possesses reduced RNase H activity, and/or reduced terminal transferase activity and/or increased fidelity. Therefore, claim 19

of the 09/845,157 application is a species of claims 91 and 111 in that it contains an added limitation of possesses reduced RNase H activity, and/or reduced terminal transferase activity and/or increased fidelity.

Further, claim 22 of the 09/845,157 application is a species of claim 100, since it is drawn to a Thr197 being replaced with glutamic acid and claim 23 of the 09/845,157 application is a species of claims 107 and 110, since it is drawn to a Phe 309 being replaced with asparagine. Claims 25, 26 and 28 of the 09/845,157 application are also species of claims 91 and 111, containing added limitations of replacing Tyr64, Arg116, Gln190 and Val223. Claim 29 is a species of claims 112, 114 and 115, 117, 119 and 120, since it contains the limitation of Glu562 being replaced with glutamine and Asp583 being replaced with asparagines.

Therefore, claims 91, 100, 107, 110, 111, 112, 114 115, 117, 119 and 120 of the instant application are generic to claims 19, 20, 22, 23, 25, 26, 28 and 29 of copending Application No. 09/845,157, or, in other words, claims 91, 100, 107, 110, 111, 112, 114 115, 117, 119 and 120 of the instant application are anticipated by claims 19, 20, 22, 23, 25, 26, 28 and 29 of copending Application No. 09/845,157.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. No references were found teaching or suggesting claims 93, 95, 97, 99, 101, 103, 110, 113-115 and 118-120, but they are rejected for reasons given above. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

July 7, 2004

Teresa Strzelecka
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